1635

**CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on **May 7, 2004**.

April Reeves

April Reeves

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

E. Raschke *et al.*

Application No.: 09/844,662

Filed: April 27, 2001

For: METHODS FOR BINDING AN EXOGENOUS MOLECULE TO CELLULAR CHROMATIN

Examiner: R. Schnizer

Group Art Unit: 1635

Confirmation No.: 9004

**TRANSMITTAL**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed please find the following:

1. Response to Restriction Requirement: 7 pages
2. Substitute Information Disclosure Statement: 4 pages
3. Return postcard

Please direct all communications regarding this application to the undersigned at the address given below.

Respectfully submitted,

Date: May 7, 2004

By: Sean Brennan

Sean M. Brennan
Registration No. 39,917

Sangamo BioSciences, Inc.
501 Canal Blvd., Suite A100
Richmond, California 94804

Telephone: (510) 970-6000 ext. 252
Facsimile: (510) 236-8951

**CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 7, 2004

April Reeves

April Reeves

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

E. Raschke *et al.*

Application No.: 09/844,662

Filed: April 27, 2001

For: METHODS FOR BINDING AN EXOGENOUS MOLECULE TO CELLULAR CHROMATIN

Examiner: R. Schnizer

Group Art Unit: 1635

Confirmation No.: 9004

## RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the Restriction Requirement dated April 7, 2004 for which a response is initially due on or before May 7, 2004. Accordingly, this response is timely filed and no fee is believed to be due.

**Remarks** begin on page 2 of this paper.

## REMARKS

### Status of the claims

Claims 1-56 were initially presented with the application as filed. In a Preliminary Amendment dated and mailed on October 10, 2002 and received in the USPTO on October 15, 2002, claim 21 was amended; claims 4, 5, 19, 25, 26 and 28-56 were cancelled and new claims 57-86 were added. In a second preliminary amendment mailed on May 20, 2003 to enter a sequence listing, the amendment of claim 21, the cancellation of claims 4, 5, 19, 25, 26 and 28-56, and the addition of claims 57-86 was reiterated. Upon notification by the Examiner that the October 10, 2002 Preliminary Amendment had not been entered into the file, a copy of this paper was mailed to the Office on June 4, 2003. Accordingly, claims 1-3, 6-18, 20-24, 27 and 57-86 are presently pending in the application.

### Information Disclosure Statement

Applicants note that three information disclosure statements have been submitted in the case (August 5, 2002, June 27, 2002 and May 3, 2002). Applicants respectfully request that the references be considered. Attached hereto is a substitute 1449 form for the IDS submitted on May 3, 2002, in which reference AO-1 was incorrectly cited as published in "Current Biology." The proper reference, published in the journal "*Chem. & Biol.*" was included with the earlier IDS and is properly listed on the substitute page enclosed herewith.

### Restriction Requirement

The claims have been restricted as follows:

**Group 1:** methods for binding an exogenous protein to a binding site in cellular chromatin. (Claims 6, 7, 9-11, 20-24, 27, 79-81 and 83)

**Group 1a:** methods for binding an exogenous protein to a binding site in cellular chromatin by introducing said protein into a cell. (Claims 6, 7, 9-17, 20-24, 27 and 79-81)

**Group 1b:** methods for binding an exogenous protein to a binding site in cellular chromatin by introducing a nucleic acid that expresses said protein into a cell. (Claims 11-17, 20 and 83)

**Group 2:** methods for binding an exogenous nucleic acid to a binding site in cellular chromatin. (Claims 75 and 76)

**Group 3:** methods for binding an exogenous small molecule therapeutic (non-protein, non-nucleic acid) to a binding site in cellular chromatin. (Claim 78)

**Group 4:** a complex between an exogenous nucleic acid and a binding site in cellular chromatin. (Claims 58 and 59)

**Group 5:** a complex between an exogenous small molecule therapeutic (non-protein, non-nucleic acid) and a binding site in cellular chromatin. (Claim 61)

**Group 6:** a complex between an exogenous protein and a binding site in cellular chromatin. (Claims 62-64, 67 and 68)

**Linking claims**

Claims 1-3, 12-18, 72-74, 77, 82 and 84-86 are stated to link Groups 1, 2 and 3.

Claims 57, 60, 65, 66 and 69-71 are stated to link Groups 4, 5 and 6.

**Traversal of the Requirement**

1. *Restriction Requirement is unclear*

Initially, Applicants note that the Restriction Requirement is unclear in several respects. First, claims 12-17 are stated to be linking claims, but are also listed in both Groups 1a and 1b. Claim 8 has not been assigned to any group, nor has it been identified as a linking claim.[1] The identification of claim 18 as a linking claim is believed to be incorrect, inasmuch as it depends from claim 10, which has been assigned to Group 1a.

Any determination of independence or distinctness of the pending claims, by the Examiner, may have later ramifications during the prosecution of this and related applications. For example, it is not entirely clear what consequences the outstanding Restriction Requirement would have relative to double patenting issues during the

[1] Inasmuch as it depends from claim 6, it is believed that claim 8 would have been assigned to Group 1a.

prosecution of non-elected claims in a related application. Accordingly, clarification is requested.

2. *Restriction between different types of exogenous molecule is improper*

Applicants submit that the Office has not met its burden in establishing the two criteria that must be met in order for restriction requirement to be proper under M.P.E.P. § 803, namely (1) the inventions must be independent or [*sic*] distinct as claimed; and, in addition, (2) there must be a serious burden on the Examiner if restriction is not required.

In support of restriction among Groups 1, 2 and 3, the Examiner asserts that the different molecules "have different modes of operation because they rely upon different exogenous molecules, *i.e.*, proteins, nucleic acids or non-proteins..." (Restriction Requirement, page 4). Likewise, the complexes of Groups 4, 5 and 6 are also alleged to differ in structure and function. *Id.*

In response, Applicants note that the claims are clearly not independent, and Applicants submit that the Examiner has not demonstrated that the subject matter of the claims are distinct from one another. It is stated in regard to Groups 1-3 generally that they are distinct inventions because "they have different modes of operation because they rely upon different exogenous molecules, *i.e.*, proteins, nucleic acids, or non-protein, non-nucleic acid small molecule therapeutics, that rely upon different or unknown binding interactions to exert their effects." (Restriction Requirement, page 4).

Applicants respectfully disagree. The Office appears to have placed undue emphasis on the relatively small number of claimed species of exogenous molecules, while ignoring the fact that, if an accessible region is identified, it can be used as a binding site for any exogenous molecule. In other words, the use of an accessible region in cellular chromatin as a site for binding of an exogenous molecule does not depend on the nature of the DNA-binding molecule.

Moreover, it is improper for the Office to prevent an Applicant from claiming what they believe to be their invention, unless the subject matter of a claim lacks unity (MPEP 803.02). In the present case, the pending claims possess unity because they share a common utility (binding of an exogenous molecule to DNA) and share a structural

feature essential to that utility (an accessible region of cellular chromatin[2]). Finally, Applicants believe that a search for DNA-binding molecules (required for the examination, *e.g.*, of linking claim 1) will necessarily reveal all types of DNA-binding molecules. Thus, restriction based on the nature of the DNA-binding molecule will not lessen the Examiner's search burden.

In sum, the Examiner has not shown that the claimed subject matter is independent and distinct (35 U.S.C. § 121), nor has it been shown that examination of all claims together would impart a serious burden. To the contrary, examination of all claims in one application would, in fact, save the Examiner time. In light of the Office's concerns about increasing numbers of applications, examination of the pending claims in a single application (rather than in six or seven separate applications) would also save Patent Office resources.

The foregoing arguments are applicable both to the method claims of Groups 1, 2 and 3 and to the composition claims of Groups 4, 5 and 6. Accordingly, Applicants urge that, at the least, all method claims be placed in a single group and all composition claims be placed in a single group.

3. *Restriction between proteins and their encoding nucleic acids is improper*

Methods of binding a protein to an accessible region in cellular chromatin involving introduction of the protein into a cell (Group 1a) and methods of binding a protein to an accessible region in cellular chromatin involving introduction, into a cell, of a nucleic acid encoding the protein (Group 1b) are alleged to be distinct without any supporting remarks.

Applicants maintain that the Office has not established that the protein delivery claims of Group 1a are distinct from the nucleic acid delivery claims of Group 1b. Although the Examiner does not address the alleged distinction between proteins and nucleic acids with respect to Groups 1a and 1b, Applicants note that all nucleic acids of Group 1b encode DNA-binding proteins. Furthermore, the nucleic acids recited in the claims of Group 1b do not, in and of themselves, bind to an accessible region in cellular

[2] *See*, for example, page 13, line 10 through page 15, line 2 of the specification

chromatin. Rather, they encode one of the recited proteins, that in turn binds to a site in an accessible region, when the nucleic acid molecule is expressed. *See, e.g.,* claim 11. Therefore, proteins and nucleic acids encoding these proteins do, by definition, rely on the same binding interactions to exert their effect. Accordingly, the Office's assertion that methods involving proteins are distinct from methods involving nucleic acids encoding these proteins is unsupported.

If the Restriction Requirement is maintained, Applicants respectfully request that the Office provide evidence that the binding interaction of a peptide encoded by a nucleic acid introduced into a cell would be materially different than the binding interaction of the same peptide, introduced into a cell in peptide form.

4. *Restriction between process of making and product is improper*

In addition, the separation between Groups 1-3, on the one hand, and Groups 4-6, on the other, is traversed. The Restriction Requirement acknowledges that these two sets of groups are related as process of making and product made, but asserts that they are distinct because the claimed product can be made by another materially different process. Specifically, the Office states that the compositions of Groups 4-6 can be obtained from naturally-occurring cells in which transcription factors, nucleic acid primers or naturally-occurring small molecules are bound to a binding site.

In response, Applicants note that the product as claimed recites a complex between an exogenous molecule and a binding site in cellular chromatin (*see, e.g.*, claim 57). Isolation of a transcription factor-DNA complex, a nucleic acid-DNA complex such as a replication primer, or a naturally-occurring small molecule-DNA complex would not provide a complex between an exogenous molecule and cellular chromatin, for two reasons. First, any complex so isolated would not comprise an exogenous molecule; second, any complex so isolated would not comprise cellular chromatin, since it would have been isolated from the cell.

Accordingly, Applicants maintain that the Office has not met its burden of showing that the compositions of Groups 4-6 are distinct from the methods of groups 1-3, and urge that restriction therebetween be withdrawn.

**Provisional election**

Solely for the purpose of compliance with 37 C.F.R. § 1.143, **Group 6** is provisionally elected. If the Restriction Requirement is made final, Applicants understand that claims 57, 60 and 62-71 will initially be examined. Applicants request confirmation that, if any of linking claims 57, 60, 65, 66 or 69-71 are allowed, the Restriction Requirement among Groups 4-6 will be withdrawn (MPEP 809) and all claims in Groups 4, 5 and 6, including any and all allowed linking claims, will be examined.

Applicants note that the process claims of Groups 1a, 1b, 2 and 3 contain all of the limitations of the elected product claims. Accordingly, if the Restriction Requirement is made final, and an elected product claim is found allowable, Applicants understand that Groups 1a, 1b 2 and 3 will be rejoined and examined (MPEP 821.04).

**CONCLUSION**

For the reasons noted herein, Applicants request reconsideration and withdrawal of the Restriction Requirement. Applicants reserve their right under 35 U.S.C. § 121 to file one or more divisional applications directed to nonelected subject matter during the pendency of this application. Should the Restriction Requirement be made final, Applicants reserve their right, pursuant to 37 C.F.R. §§ 1.144 and 1.181, to petition the Requirement at any time during the pendency of this application, prior to appeal.

Respectfully submitted,

Date: May 7, 2004

By: Sean Brennan

Sean M. Brennan
Registration No. 39,917

Sangamo BioSciences, Inc.
501 Canal Blvd., Suite A100
Richmond, California 94804
Telephone: (510) 970-6000, ext. 252
Facsimile: (510) 236-8951